REVIEW
OF
LITERATURE
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Cancer of the prostate is the second most common malignancy in men, and in men older than age 55 years, it is the third most common cause of cancer deaths (after carcinomas of the lung and colon).

Cancer of the prostate is a disease of aging. It is rarely diagnosed in a man younger than 50 years, and its incidence increases progressively thereafter until a peak occurs in the eighth decade. In the USA, about 75,000 cases are diagnosed annually, and about 24,000 deaths occur each year as a direct result of the disease. Because the male population over age 50 is steadily increasing in numbers and because there is some evidence to suggest an increase in the incidence of prostate cancer, the number of cases diagnosed yearly is expected to exceed 125,000 by the year 2000. Moreover, 3-8 times more cases go unrecognized clinically and are apparent only upon incidental autopsy examination of the prostate or at the time of prostatectomy for benign disease. These "latent" or clinically unrecognized cases present a much larger population of men in whom the disease is of a very low malignant potential or in whom death from other causes
intervenes before sufficient time has elapsed to allow for full expression of the prostatic cancer. In the future, with more sophisticated methods of detection, many of these "sub-clinical" cases will be clinically diagnosed, adding even further to the magnitude of the problem of prostate cancer.

The exact size of the pool of men with prostatic cancer is difficult to determine. RICH (1935) reported that the disease was recognized clinically prior to death in only one-third of patients found to have prostatic cancer at the time of autopsy. By carefully examining step sections of the prostate gland, FRANKS (1954) observed that 30% of men older than 50 years who died of other causes had histologic evidence of prostatic carcinoma. The incidence was 40% in men 70-79 years of age and 67% in men 80-89 years. Similar results have been found in analyses of material obtained at the time of transurethral resection of the prostate for benign disease. SHELDON et al (1980) reviewed the literature and reported the following average incidence rates of prostatic cancer discovered incidentally in men undergoing transurethral resection of the prostate: 10.4% in those 50-59 years of age, 18.5% in those 60-69 years, and 28.7% in those 70-79
years.

The treatment modality and prognosis largely depend on 'stage' and/or 'Grade' of cancer prostate. The cancer start developing in peripheral zone of prostate in most of cases and so 'PROSTATISM' appears only late. However, many a times a hard nodule or nodules can easily be palpated on the surface of prostate gland during per rectal examination, suggesting malignancy. But by no means, a hard nodule is pathognomonic of malignancy. (It can also be found in totally benign conditions of the prostate, gland and nearby structures, e.g. chronic prostatitis, granulomatous prostatitis, prostatic calculi, chronic seminal vesiculitis etc.). Site, size and number of nodule(s) is not contributory in the diagnosis of carcinoma prostate.

A palpable nodule of abnormal induration is malignant in only 50% of cases (JEWETT H.J.) and so clinical examination is certainly not a worth while' manner to establish the diagnosis of early prostatic carcinoma. All methods, other than prostatic biopsy, are non-specific in early detection of cancer prostate.

A transrectal probe is used for pelvic sonography, carcinoma is manifested by asymmetric densities within the prostate. The
procedure is not a sensitive means of establishing a diagnosis but is useful for documenting the degree of extension of the tumor into bladder and seminal vesicles. Computerised tomography (CT) of the prostate may also be helpful in defining the extent of tumor and locating nodes for aspiration needle biopsy. (ARTHUR I. SAGALOWSKY, JEAN D. WILSON IN HARRISON'S PRINCIPLES OF INTERNAL MEDICINE).

Several biochemical markers provide ancillary information in diagnosing, prostatic cancer. Elevated serum acid phosphatase occurs in some patients with localized carcinoma and more commonly in patients with bony metastases. However, no technique of assay for the enzyme (including counterimmune electrophoresis and radioimmuno assay) is sufficiently specific or sensitive for use in screening, and the major application of the assay is in following the progress of the disease after the diagnosis is established. Likewise, none of the other plasma makers studied - bone marrow acid phosphatases, carcinoembryonic antigen, lactic dehydrogenase, creatinine phosphokinase, hydroxyproline, cholesterol isoleucine, glycine, aspartic acid, glutamic acid, methionine, or spermidine has sufficiently high specificity or
sensitivity for routine screening. Experiences with newly detected tumor marker, prostate - specific antigen (PSA) (By KURIYAMA et al 1982) in early detection of carcinoma prostate are still in preliminary stage, and so we are left with prostatic biopsy, which gives us - diagnosis, as well as grading of carcinoma prostate.

There are several methods for taking a biopsy from this relatively poorly accessible organ; but it is only needle biopsy, and that too, fine needle aspiration biopsy from transrectal route, which contains a privilege to be accepted widely to all, namely the patient, the surgeon and the pathologist.

Thick or core biopsy needles are less acceptable to patient, more traumatizing, and cannot screen the prostate gland widely. (As FNAC can certainly do!) Open perineal biopsy carries risk of at least temporary impotence and is a more extensive surgical procedure, and so cannot be used routinely. Transurethral biopsy is also not of much use because most early lesions are in the peripheral regions of the prostate.

The concept of taking a little tissue for biopsy by needle is not new, and was known to VELPRAU (1856): "There would be so little danger in extracting a small quantity of tissue from an obscure
growth by the aid of a needle trocar or cannula, so little substance is there necessary for the microscope that the diagnosis of cancer would no longer be embarrassing or vague.

This concept was revived by MARTIN and ELLIS and was further developed at Memorial Hospital for Cancer in New York city. Thereafter, RUSSELL FERGUSON, a urologist at Memorial Hospital took the lead and became amongst the first in performing aspiration biopsies of the prostate gland; but the credit of popularizing the aspiration biopsy of the prostate goes to Sixten Franzen (1960) and his associates at Sweden's Karolinska Institute. They DESCRIBED A NEW BIOPSY DEVICE CONSISTING OF FLEXIBLE NEEDLE GUIDE AND POPULARIZED A METHOD FOR OBTAINING TRANSRECTAL ASPIRATION SPECIMENS ON AN OUTPATIENT BASIS. THESE INITIAL REPORTS DESCRIBED SMEARS THAT WERE AIR-DRIED AND STAINED BY THE MAY-GRUENWALD-GIEMSA STAIN. TWENTY YEARS AFTER THESE INITIAL CONTRIBUTIONS, JAN SILVESTER WILLEMS AND TORSTEN LOWHAGEN REPORTED THAT APPROXIMATELY 750 PROSTATIC ASPIRATION BIOPSIES WERE BEING PERFORMED ANNUALLY AT THE KAROLINSKA
HOSPITAL AND THAT ABOUT 30 PER CENT OF THESE SPECIMENS WERE DIAGNOSTIC OF PROSTATIC CARCINOMA.

It is the Franzen method of taking fine needle aspiration biopsy from the prostate gland by transrectal route that attained maximum popularity and has become a standard procedure and is in common use currently.

THE FOLLOWING ENTITIES MUST BE CONSIDERED IN THE EVALUATION OF PROSTATIC ASPIRATES: (1) INFLAMMATORY DISORDERS NONSPECIFIC CHRONIC PROSTATITIS AND GRANULOMATOUS PROSTATITIS, (2) HYPERPLASIA: (3) INFARCTS: (4) ADENOCARCINOMAS OF ACINAR AND DUCTAL ORIGIN: and (5) OTHER MALIGNANT TUMORS (RARE TUMORS OF PROSTATIC ORIGIN, TUMORS OF ADJACENT ORGANS INVADING PROSTATE, AND METASTASES FROM DISTANT SITES).

THIS RELATIVELY SMALL NUMBER OF DISEASES RESULTING IN PALPATORY ABNORMALITIES RENDERS THE EVALUATION OF PROSTATIC ASPIRATES RELATIVELY UNCOMPLICATED. FOR ALL PRACTICAL INTENTS AND

TRANSRECTAL ASPIRATION BIOPSY SHOULD BE PERFORMED TO EXAMINE PROSTATE GLANDS WITH, (1) PALPABLE DISCRETE NODULES: (2) INDURATION: (3) FIXATION: (4) BENIGN ENLARGEMENT, ESPECIALLY PRIOR TO TRANSURETHRAL RESECTION: (5) SONOGRAPHIC ABNORMALITIES SUGGESTIVE OF CARCINOMA (6) INCIDENTALLY DETECTED ELEVATIONS IN PROSTATE TUMOR MAKERS SUCH AS PROSTATE-SPECIFIC ACID PHOSPHATASE OR PROSTATE-SPECIFIC ANTIGEN: (7) FOR THE EVALUATION OF METASTATIC ADENOCARCINOMA WITH AN UNKNOWN PRIMARY; AND (8) AS AN OBJECTIVE AND REPRODUCIBLE PROCEDURE FOR DETERMINING THE EFFECT OF TREATMENT ON THE PRIMARY TUMOUR IN CASES OF PROSTATE CARCINOMA NOT MANAGED OPERATIVELY (JOHN A MAKSEM, CHANHO H. PARK, PAUL W.
JOHENVING CIRILO F. GALANG AND MYRON TANNENBAUM 1988).

They recommended "that the method to be used to evaluate glands even minimally abnormal by digital rectal examinations; but did not recommend biopsy of the normal prostate gland as a screening procedure.

According to ESPOSTI P.L. (1974) ALTHOUGH GLANDS WITH SUSPECTED PROSTATIS SHOULD BE EVALUATED WITH THE UTMOST CAUTION, BEARING THE SAFETY OF THE PATIENT IN MIND, PROSTATIS SHOULD NOT BE CONSIDERED AN ABSOLUTE CONTRAINDICATION TO THE PROCEDURE. ALTHOUGH PROSTATIS CAUSES PALPABLE ABNORMALITIES IN OTHERWISE BENIGN PROSTATE GLANDS, IT IS NONETHELESS FREQUENTLY ASSOCIATED WITH OUTRIGHT MALIGNANCY (14.1% In a series reported by JOHN A. MAKSEM et al, and about 10% in a series reported by ESPOSTI).

Cytology preparation afford a view at right angles, to the generally seen in histology preparations: epithelial cells are seen en face. In this arrangement, the cells of the prostatic epithelium lie
in an orderly sheet-like pattern, and cell borders, especially at the apical intercellular zone, assume a distinct honeycomb configuration. In hyperplastic epithelium, clusters of epithelial cells from papillae that rise out of the plain of the epithelial sheet, forming on low-power examination, “hills and valleys” or club like arrangements. In epithelial atrophy of the prostate, a change that may accompany stormal hyperplasia, cellular epithelium is more cuboidal, and cell boundaries are distinct without the prominent atypical scalloping of cytoplasm towards the luminal surface. In all benign epithelial patterns, the nuclei of the cell are similar, being regularly distributed rather monotonous, unilayered and round to oval. The chromatin pattern is finely granular, and the nuclear size is similar to that of an erythrocyte. Nucleoli of benign epithelial cells are generally indistinct except in occasional cases of epithelial hyperplasia, in which chromocenters or micronucleoli may be seen.

Immediately below the epithelial layer are haphazardly clustered fusiform nuclei that appear in various packing densities. These belong to the basal cells of the prostate. Basal cells are present in normal, atrophic and hyperplastic epithelium. In atrophic
epithelium, they are more dense, than in normal state. In hyperplastic glands, an increase in the number of basal cells may be seen, and their unclear countours may appear enlarged and more rounded. In dysplasia (atypical epithelial hyperplasia, prostatic interepithelial neoplasia), the density of the basal cells show crude inverse proportionality to the degree of the lesion.

THE FEATURES THAT DIFFERENTIATE ADENOCARCINOMA FROM BENIGN EPITHELIAL PATTERNS OR REACTIVE EPITHELIAL ATYPIA INCLUDE THE MAJOR CRITERIA APPLIED TO MOST MALIGNANCIES; CELLULARITY, DYSHESION, VARIATION IN NUCLEAR SIZE (ANISONUCLEOSIS) AND SHAPE (POIKINONUCLEOSIS), AND NUCLEOLAR PROMINENCE. THE CYTOMORPHOLOGY OF PROSTATE CANCER IS DEPENDENT ON ITS DEGREE OF DIFFERENTIATION- THAT IS, THE EXTENT OF THE TUMOUR’S RESEMBLANCE TO BENIGN PROSTATIC GLANDULAR TISSUE- AND THE DEGREE OF ANAPLASIA- THAT IS, NUCLEAR ABNORMALITIES. AS A GENERAL RULE, DECREASING DIFFERENTIATION IS ACCOMPANIED BY INCREASING ANAPLASIA, ALTHOUGH ASPECTS OF
DIFFERENTIATION AND ANAPLASIA MAY BE ADDRESSED SEPARATELY IN CYTOLOGY SPECIMENS OBTAINED BY ASPIRATION BIOPSY. IN GENERAL, THE CYTOLOGIC GRADING OF ASPIRATION BIOPSY SPECIMENTS OF THE PROSTATE HAS BEEN BASED ON DEGREE OF NUCLEAR ANAPLASIA WITH PERHAPS TWO EXCEPTIONS – THE RECOGNITION OF MICROADENOMATOUS COMPLEXES IN HIGHLY DIFFERENTIATED CARCINOMAS AND OF CELLULAR DISSOCIATION WITH POORLY DIFFERENTIATED CARCINOMAS.

THE UROPATHOLOGICAL STUDY GROUP ON PROSTATIC CARCINOMA HAS ADDRESSED THREE DEGREE OF CHANGE (SLIGHT, MODERATE AND SEVERE) AMONG SIX NUCLEAR FEATURES: AVERAGE NUCLEOLAR SIZE, NUCLEOLAR VARIABILITY (SIZE, SHAPE, NUMBER), DISTURBANCE OF NUCLEAR ARRANGEMENT, AND CELLULAR AND NUCLEAR DISSOCIATION. EACH CRITERION IS ASSESSED AND SCORED, AND THEN THE SCORES ARE ADDED, GIVING A BEST POSSIBLE OVERALL SCORE OF 6 AND A WORST POSSIBLE OVERALL SCORE OF 18. SCORES
OF 6 TO 1- CORRESPOND TO GRADE I, OF 11 TO 14 TO GRADE II, AND OF 15 TO 18 TO GRADE III, THAT IS, WELL, MODERATELY, AND POORLY DIFFERENTIATED CARCINOMAS.